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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/613,767	07/03/2003	Fu-Sheng Wang	11333/20	4833

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EXAMINER

SCHUBERG, LAURA J

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 07/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/613,767

Applicant(s)

WANG ET AL.

Examiner

Laura Schuberg

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 7, 8, 12 and 20-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 9-11, 13-19 and 23-25 is/are rejected.
- 7) ☒ Claim(s) 19 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>12/04/2003</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the following species: "side scattered light and fluorescent light emitted by the cell" as the species of morphological information; "a cell induced from a CD34 positive hematopoietic cell" as the species of purified megakaryocyte; and combination of "cell interior information" and "cell staining information" as the species of information from the cell, in the reply filed on 05/18/2006 is acknowledged.

Claims 7, 8, 12, 20-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected specie, there being no allowable generic or linking claim.

Claims 1-6, 9-11, 13-19, 23-25 have been examined on the merits.

Claim Objections

Claim 19 is objected to because of the following informalities: The term "base" in line three should be "based". Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 10, 11, 13-17, 19, 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Tomer et al (Blood 1988) in light of Jing et al (Chinese Medical Journal 2002) and Houwen et al (US 5,830,701).

Claim 1 is drawn to method of detecting a megakaryocyte comprising: providing a sample comprising a cell; detecting a plurality of morphological information; generating a scattergram and determining whether a population exists in a megakaryocyte region of the scattergram.

Claims 2 and 4 are drawn to preparation of an assay with a fluorescent dye.

Claim 3 is drawn to wherein the detecting involves an automated hematology analyzer.

Claim 6 is drawn to wherein the plurality of morphological information comprises side scattered light and fluorescent light emitted by the cell.

Claim 10 is drawn to identifying the megakaryocyte region of the scattergram.

Claim 11 is drawn to claim 10 wherein the identifying comprises 2 reference scattergrams, one with purified megakaryocytes and one substantially free of megakaryocytes and comparing them.

Claims 13 and 14 are drawn to claim 11 wherein the purified megakaryocyte comprises a cell induced from a CD34 positive hematopoietic cell by thrombopoietin.

Claim 15 is drawn to a method of detecting a megakaryocyte comprising: preparing an assay sample by combining a sample comprising a cell with a reagent; detecting a plurality of information from the cell, wherein the information is selected from

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the group consisting of cell size, cell interior, degree of cell staining and combinations thereof; generating a scattergram by plotting the plurality of information and determining whether a population exists in a megakaryocyte region of the scattergram.

Claim 16 is drawn to wherein the detecting involves an automated hematology analyzer.

Claim 17 is drawn to wherein the reagent comprises a fluorescent dye.

Claim 19 is drawn to wherein the cell interior information is based on side scattered light emitted by the cell, and the degree of cell staining information is detected based on fluorescent light emitted by the cell.

Claim 23 is drawn to a method of detecting a megakaryocyte comprising preparing an assay sample by combining a sample comprising a cell with a reagent comprising a fluorescent dye and a hemolytic agent; detecting scattered light and fluorescent light emitted by the cell; generating a scattergram by plotting the scattered and the fluorescent light; determining whether a population exists in a megakaryocyte region of the scattergram.

Claim 24 is drawn to wherein the scattered light comprises side scattered light.

Claim 25 is drawn to wherein the detecting involves an automated hematology analyzer.

Tomer teaches a method of detecting megakaryocytes that includes preparing an assay sample by combining bone marrow from normal human donors (p.1244 column 2) with fluorescent antibodies (dye) and a hemolytic agent (0.1% sodium citrate) (p.1245 column 1)(claims 2, 4, 15, 17, 23). The 0.1% sodium citrate is a hemolytic agent

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because it is hypotonic and will cause the red blood cells to lyse. Data collection of the fluorescence intensities and scattered light of each cell are carried out (p.1245 column 2)(claims 1, 6, 15, 23). Scattergrams are generated by plotting scattered light and fluorescent light (p.1246 column 1) (claims 1, 15, 23). A megakaryocytic region is identified in the scattergrams by generating 2 reference scattergrams, one with purified megakaryocytes and the other without (p.1246 column 1) (claims 1, 10, 11,15, 23). A population is determined to exist in a megakaryocytic region of the scattergram. The cell interior information is detected based on side scattered light and the degree of cell staining information is detected based on fluorescent light emitted by the cell (p.1244 column 2) (claims 19, 24). An automated hematology analyzer is also taught (p.1244 column 2) (claims 3, 16, 25).

The purified megakaryocytes are inherently induced from CD34 positive hematopoietic cells (Houwen US 5,830,701, figure 9) by thrombopoietin (TPO) (as supported by Jing et al, p.983 column 1) and this induction occurs *in vivo*. Since the claim language does not require the induction to be *in vitro*, this meets the limitations of claims 13 and 14 as claimed.

The disclosure by Jing and Houwen are supporting references and properly used in a rejection under of U.S.C. 102 since they describe that megakaryocytes are inherently induced from CD34 positive cells by thrombopoietin *in vivo*. MPEP 2131.01.

Claims 1-3, 5, 9, 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Houwen et al (US 5,830,701).

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Claims 1-3, and 10 are drawn to the method of detecting a megakaryocyte as described above.

Claim 5 is drawn to wherein the preparing of the assay sample does not involve an immunological method.

Claim 9 is drawn to wherein the detecting comprises passing the assay sample through an electrically charged aperture and identifying a change in direct current resistance and radio frequency resistance.

Houwen teaches a method of detecting hematopoietic progenitor cells which comprises treating a blood sample with a reagent which detects immature cells without employing any immunological techniques; obtaining cell information about the treated blood sample using a particle analyzer and constructing a cell distribution profile (scattergram); delineating a portion of the profile as a zone in which at least one subclass of hematopoietic progenitor cells appear; wherein the profile zone is delineated through the use of a control sample comprising hematopoietic progenitor cells and counting the cells in the zone (column 11)(claims 1, 2, 5, 10) . Hematopoietic progenitor cells (HPC) are taught to consist of many subclasses, including CFU-Meg (megakaryocytes). The use of a reagent that can lyse erythrocytes (hemolytic) is also taught (column 4 line 63). Where the detecting comprises passing the assay through an electrically charged aperture and identifying a change in direct current (DC) resistance and radio frequency (RF) resistance is taught as well as cell size information based on a change in DC and cell interior information based on a change in RF (column 7 lines 2-

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23)(claim 9). The use of an automated hematology analyzer is taught as well (column 7 line 51)(claim 3).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15, 16, 18, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakata (Sysmex Journal International 2000) in view of Houwen (US 5,830,701), Walters et al (Laboratory Hematology 2000) and Ota et al (Haematologia 2000).

Claims 15, 16, 23 and 25 are drawn to the method of detecting a megakaryocyte as described above. (Applicant has elected the combination of cell interior information and degree of cell staining information as the species of cell information.)

Claim 18 is drawn to wherein the preparing of the assay sample does not involve an immunological method.

Sakata teaches a method of detecting nucleated red blood cells (NRBC) with a reagent that comprises a fluorescent dye (polymethine) and a hemolytic agent (p.41). Scattered light and fluorescent light are detected and a scattergram is generated (p.44). The detecting involves an automated hematology analyzer (XE-2100) (p.41). The preparing of the sample does not involve an immunological method. In addition, Sakata teaches that in the Xe-2100, by developing and using optimum polymethine dyes not only for the NRBC channel, but also the 4 DIFF and RET channels, a wide variety of normal and abnormal cells can be classified and counted (p.42 column 2). Sakata also

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teaches that the automated hematology counter will be able to count all types of cells- including, in the future, cells presently considered to be "impossible" to count (p.45).

Sakata does not teach the use of the method to detect megakaryocytes or to determine if a population exists in a megakaryocyte region of a scattergram.

Houwen teaches the use of the automated hematology analyzer, SE-9000 (column 7 line 51), for the detection of megakaryocytes (column 4 line 35) and for the determining of the region of the scattergram where the megakaryocyte population exists (column 7 lines 53-55). The use of a flow cytometer operating on an optical principle is taught as an alternative particle analyzer (column 7 line 17). Houwen also teaches that there is a great benefit to the medical field in monitoring of hematopoietic progenitor cells (which includes megakaryocytes) in peripheral blood stem cell transplantation (column 11 lines 1-4).

Walters teaches that a comparison between hematology analyzers Sysmex XE-2100 and Sysmex SE-9000 showed excellent correlation for all parameters except number of basophils (p.89). Walters also teaches that the Sysmex XE-2100 has proven to be an accurate and precise high-speed analyzer and is suitable for both high volume laboratories and laboratories that test many abnormal samples (p.92).

Ota teaches that violet polymethine dye (VPM) is a megakaryocyte-specific stain that is clinically useful for estimating of megakaryocyte count, classification of megakaryocytes and identification of immature megakaryocytic cells (p.21).

One of ordinary skill in the art would have been motivated to use the method of Sakata for the detection of megakaryocytes because Sakata suggests that the method

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could be used for other cell types than NRBs (p.42 column 2 and p.45 column 1) and Houwen teaches that there is a great benefit to the medical field in monitoring of megakaryocytes (column 11 lines 1-4). One of ordinary skill in the art would have been motivated to identify a megakaryocytic region in the scattergram generated by the method of Sakata because regions for other cell types are also generated. One of ordinary skill in the art would have had a reasonable expectation of success because Walters teaches that the Sysmex XE-2100 (used by Sakata) showed excellent correlation with the Sysmex SE-9000 (used by Houwen to detect megakaryocytes) and Ota teaches that a polymethine dye (also used by Sakata) is specific for megakaryocytes allowing detection of megakaryocytes.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 5, 9, 10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 8-12 of U.S. Patent No. RE39,006 E in view of Tomer et al (Blood 1988). U.S. Patent RE39,006 E teaches all the claimed limitations except for that the hematopoietic progenitor cells detected are megakaryocytes. Tomer teaches that the detection of megakaryocytes is applicable to studies of pathologic states (p.1251 column 2).

Therefore, one of ordinary skill in the art would have been motivated to use the method of patent RE39,006 for the detection of megakaryocytes because Tomer teaches that this would be applicable to studies of pathologic states. One of ordinary skill in the art would have had a reasonable expectation of success because patent RE39,006 is drawn to using hematopoietic progenitor cells (HPC) and megakaryocytes are a type of HPC.

Conclusion

No claims are allowed.

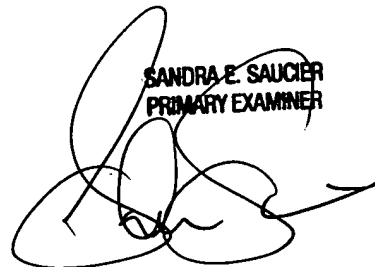
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura Schuberg whose telephone number is 571-272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Laura Schuberg


SANDRA E. SAUCIER
PRIMARY EXAMINER